ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

ahfmr research news

WINTER 2002

Making babies better

On the Cover

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AHFMR Mission

AHFMR supports a community of researchers who generate knowledge whose application improves the health and quality of life of Albertans and people throughout the world. AHFMR's long-term commitment is to fund health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

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research news

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It can be tough convincing young women to consider careers in science or engineering when entering university but major strides have been made. Just ask Dr. Elizabeth Cannon and Dr. Margaret-Ann Armour. Both Alberta university professors have spent much of their professional lives trying to encourage young women to think about these options.

In 2001, when University of Calgary geomatics engineering professor Dr. Elizabeth Cannon was still the Petro-Canada/NSERC Chair for Women in Science and Engineering for the Prairies, she started an e-mail mentoring program called SCIberMENTOR. The program matches 11- to 18-year-old girls from around Alberta with young women studying science and engineering, or with practising women scientists and engineers. Now, in the third year of SCIberMENTOR, Dr. Cannon is working with social scientists to determine its impact on participants. "I think we've come a long way," she says. "The overall goal is to allow young women to make informed decisions. If science is not something they want to do, then that's fine. But they should be prepared and informed about what the options are and how that may work for them."

Generally, there are more women in science than there were 10 years ago. As many as 40% of science undergrads at Alberta universities are female. More than 50% of medical students are female. Even engineering, a field which has traditionally been dominated by men, has seen progress—22% of engineering undergrads in the province are now women.

That said, however, female participation in some disciplines within science and engineering is still weak—computer science programs and electrical engineering courses typically have only around 15% female enrolment, and the numbers in physics and mathematics are similarly low.

Moreover, only 7% of Alberta's current professional engineers are women. As the older generation of almost exclusively male engineers retire, younger female engineers will gradually make up a larger proportion of the profession. "To get the increases that we're seeing at the university making an impact on the workplace, that takes a long time," says Dr. Cannon.

"The overall goal is to allow young women to make informed decisions."

The Women in Scholarship, Engineering, Science and Technology (WISEST) program at the University of Alberta has been in existence for 20 years. It offers a number of programs at the university, including one-day workshops for girls in Grade 6 (Choices) and high school (SET), as well as the six-week WISEST summer research program that gives Grade 11 students a hands-on summer research experience in a university lab.

WISEST vice-chair Dr. Margaret-Ann Armour, who is also assistant chair of the U of A Department of Chemistry, has been involved with the program since its inception. She says the summer research program, in particular, increases the commitment of the young women to continue in sciences and engineering because they know more about the subjects and are acquainted with faculty before they enroll at the university.

"I think the disappointment for me is that we have not seen the increase, particularly in first-year university classes, continue on into faculty positions and decision-making roles," says Dr. Armour. In the University of Alberta's Faculty of Engineering, 1.9% of faculty members were women in 1981, compared to

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"We have not seen the increase continue on into faculty positions and decision-making roles."

6.5% in 2002; while in the Faculty of Science, the percentage of women faculty members was 5.1 in 1981, compared to 12.1 in 2000. "That's the area that we're the most interested in now: to determine the difficulties that face young women as they look at their career path, and why they are not ending up in the faculty positions."

While women are entering the first-year sciences in larger numbers than ever before, they're still leaving at a higher rate than men at key transition points—such as at the end of first year, after an undergraduate degree, or even after a decade in the workforce. The reasons still need to be studied, but Dr. Armour has some idea: "Women are always concerned about balancing a career and a family," she explains. "And especially going on to do graduate school, they look at the time it's going to take them to finish a Ph.D. and they begin to wonder, 'Do I really want to do this, or do I want to settle down and have a family and then come back?' Unfortunately, they don't come back very often."

More than a **bright** idea

It takes more than a bright idea to make a commercial success, and few people know this better than Dr. Fakhreddin Jamali and James Chivers-Wilson.

Both are deeply involved in bringing to market Dr. Jamali's bright idea—a discovery that boosts the effectiveness of existing pain-relief medication—via Edmonton-based EquiTech Corporation. The specialty pharmaceutical company has compelling early results, but needs to do more testing, especially in humans, in order to interest a major pharmaceutical company in becoming a development partner. More testing requires more time and more money.

"We've come very far in only two years," says Mr. Chivers-Wilson, EquiTech's president and CEO. "But raising more money is a tough job. What keeps us going is the amazing potential of this breakthrough." A recent survey of pain sufferers found that 67% were not satisfied with the effectiveness of the painkiller they use. Combine this figure with the estimated value of the global pain-medication market—$US 25 billion in 2003—and it's easy to see the potential.

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While women are entering the first-year sciences in larger numbers than ever before, they're still leaving at a higher rate than men at key transition points—such as at the end of first year, after an undergraduate degree, or even after a decade in the workforce. The reasons still need to be studied, but Dr. Armour has some idea: "Women are always concerned about balancing a career and a family," she explains. "And especially going on to do graduate school, they look at the time it's going to take them to finish a Ph.D. and they begin to wonder, 'Do I really want to do this, or do I want to settle down and have a family and then come back?' Unfortunately, they don't come back very often."

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LEFT: DR. MARGARET-ANN ARMOUR

"WHAT KEEPS US GOING IS THE AMAZING POTENTIAL OF THIS BREAK-THROUGH."

Before there was potential, however, there was science. It all started with a series of key insights into the ineffectiveness of pain-relief medication during episodes of acute pain. Dr. Jamali, a pharmacy professor at the University of Alberta known internationally for his expertise in rational drug therapy, noted that the activity of the stomach and gastrointestinal tract slows down during episodes of acute pain, in part due to suppression of the vagus nerve. This major nerve controls a number of functions in our bodies, including stomach contractions and the production of stomach acid. When stomach activity slows down in response to pain, the body's absorption of drugs also slows down.

Dr. Jamali reformulated ibuprofen—the pain relief compound in such over-the-counter analgesic medication as Motrin and Advil—so as to enhance its dissolvability under these less-than-ideal conditions. The result is a new product called ZAG-1701, a fast-acting ibuprofen that promises relief in a much shorter period of time. It is EquiTech's lead product.

ZAG-1701 has had excellent initial results in comparisons to conventional ibuprofen, delivering a greater amount of the drug in half the time. EquiTech has shared these results with a number of potential partners. "Our intent has always been to license our product to a major pharmaceutical company that operates in the pain-relief market," says Mr. Chivers-Wilson. "We're a small company; we simply don't have the money or the marketing power to take this product all the way to commercialization."

"In our conversations with potential investors and business partners, one thing became very clear—the product remains a leap of faith without human tests. The message we received was: Show us data from human trials."

So that is exactly what EquiTech is doing. With a small-scale batch of ZAG-1701 made by a contract manufacturing company, a clinical trial involving people who have just had a wisdom tooth extracted (the "industry standard" for acute pain) will likely take place in Edmonton by mid-2004. "Once we have the human data, we'll go back to our prospective partners," says Mr. Chivers-Wilson. "If all goes well, a licensing deal will follow."

AHFMR has been an important player in the development of ZAG-1701 through its Technology Commercialization (TC) program. EquiTech received TC funding to help with the costs of intellectual property protection, regulatory submissions, manufacturing of the pilot batch, and clinical trials. "The TC funding has been critical to moving ZAG-1701 from a scientific idea closer to a commercial product," says Mr. Chivers-Wilson. "Another benefit is the credibility that comes from having AHFMR as a supporter. AHFMR did its due diligence and awarded TC money to EquiTech—this is something we talk about to investors. It makes a difference."

"There is so much good science in Canada; we must get it out of the lab," says Mr. Chivers-Wilson.

"As EquiTech's story shows, there's a long road from bright idea to commercial product. It's not for the faint-hearted or the risk-averse. But I don't dwell on that. I believe in the potential we have to create something that's going to help millions of people. That's where the excitement is."

"ANOTHER BENEFIT IS THE CREDIBILITY THAT COMES FROM HAVING AHFMR AS A SUPPORTER."

Battling a glo

The global AIDS epidemic shows no signs of abating. The Joint United Nations Programme on HIV/AIDS (UNAIDS) announced recently that 40 million people around the world are infected with HIV (human immunodeficiency virus). This year alone, 5 million people became infected with HIV, and 3 million died—that's 8,000 people every day.

Like the global figures, the number of persons living with HIV in Canada is also rising: from an estimated 40,000 in 1996 to 56,000 in 2002, according to Health Canada. In 2001, about 640 Albertans had HIV, compared to 123 in 1998.

AIDS (acquired immunodeficiency syndrome) affects people of both sexes, all ages, and all social and cultural backgrounds, says Heritage Scholar Dr. Christopher Power, a physician and scientist in the University of Calgary's Faculty of Medicine. "People should not become complacent about AIDS," stresses Dr. Power, who treats general patients at the Foothills Medical Centre and AIDS patients at the Southern Alberta AIDS Clinic. "This continues to be a global epidemic that is not going away. It's getting worse."

AIDS-related dementia

These days, the new antiretroviral drug therapies for HIV/AIDS have allowed those infected with HIV/AIDS to live longer–at least those who live in the parts of the world that can afford the drugs. Sadly, as many as 90% of these HIV patients who are living longer will develop neurological disorders. Between 10% and 15% will be afflicted with AIDS-related dementia, a mental deterioration seen only in HIV-infected individuals. Patients initially experience problems with memory, concentration, motor skills, and balance; ultimately, their mental deterioration and neurological problems become debilitating. Because their immune suppression is, in most cases, already extremely advanced, people infected with HIV who develop dementia also develop other medical problems. Peripheral neuropathy, for instance, a neurological disorder resulting from damage to nerves other than the brain and spinal cord (the central nervous system), is very common in these patients.

"Dementia is devastating for these people," says Dr. Power, the only neurologist in Canada treating AIDS-related dementia. "Once people develop dementia, their survival prognosis is considerably worse."

bal epidemic

An exciting discovery

When not treating patients, Dr. Power investigates disease mechanisms and potential treatments for AIDS-related neurological diseases in the research lab. This year he and his research colleagues made an important discovery. Previous studies had shown that AIDS-related dementia results in neuronal damage within the brain. Dr. Power discovered the underlying cause—how HIV initiates this destruction: The enzyme MMP-2 is normally harmless; however, when triggered by HIV, it degrades a molecule known as SDF-1 which is required for normal brain growth and function. The degraded SDF-1 is extremely toxic and kills the surrounding brain cells.

In collaboration with Dr. Christopher Overall at the University of British Columbia, Dr. Power explored whether he could block the toxic effects of MMP-2 using drugs that are currently in clinical trials for treating cancer. Known to inhibit various proteins, the drugs did seem to protect the brain from the HIV virus and stop the AIDS-related dementia. Dr. Power hopes to investigate these drugs further as a potential therapy for patients with dementia. "This is a very interesting discovery that we're going to try to pursue therapeutically," he says. "We're trying to establish a clinical trial based on peer-review funds to extend our findings. We're also trying to identify the exact receptor by which the brain cell death occurs."

Dr. Power's discovery has enormous implications, not only for developing future treatments for AIDS patients, but also for helping patients with other types of dementia. In 2000, there were approximately 24,000 Albertans 65 or older with various types of dementia, including Alzheimer's disease. It's estimated that the number of people with this diagnosis will triple between 1991 and 2031.

A Canadian comes home

After post-doctoral training at Johns Hopkins University, Dr. Power worked at the National Institutes of Health (NIH) in Bethesda, Maryland, before moving back to Canada nine years ago. He points out that Alberta offers a great environment for research. "This kind of research could not be done without the support of the Alberta Heritage Foundation for Medical Research and other agencies," says Dr. Power. "We're trying to translate our research into better care for people. I want Albertans to know that we really appreciate their support. We can't do it without them."

Dr. Christopher Power is an AHFMR Scholar and an associate professor in the Department of Clinical Neurosciences at the University of Calgary. His research is also funded by the Canadian Foundation for AIDS Research, the Canadian Institutes of Health Research (CIHR), the Multiple Sclerosis Society of Canada, and the US National Institutes of Health (NIH).

Selected publications

Zhang K, McQuibban GA, Silva C, Butler GS, Johnston JB, Holden J, Clark-Lewis I, Overall CM, Power C. HIV-induced metalloproteinase processing of the chemokine stromal cell derived factor-1 causes neurodegeneration. *Nature Neuroscience* 2003 Oct;6(10):1064-1071.

Power C. Retroviral diseases of the nervous system: pathogenic host response or viral gene-mediated neurovirulence? *Trends in Neurosciences* 2001 Mar;24(3):162-169.

Making babies better

LIFE HANGS IN THE BALANCE EVERY DAY IN A NEONATAL INTENSIVE CARE UNIT (NICU). THE VERY SICK INFANTS CARED FOR IN THE NICU BENEFIT FROM THE NEW MEDICINES AND IMPROVED EQUIPMENT, WHICH HAVE INCREASED SURVIVAL RATES DRAMATICALLY OVER THE PAST TEN YEARS. BUT SOMETIMES EVEN THIS INTENSIVE CARE ISN'T ENOUGH.

"There are some problems we can't solve at the bedside. There are babies who just don't get better, despite our best efforts," says Heritage Clinical Investigator Dr. Bernard Thébaud, an Edmonton neonatologist (a physician specializing in the care of sick newborn babies) who works in the NICU at the Royal Alexandra Hospital and who conducts research in the Vascular Biology Group at the University of Alberta. "But just because there are no answers at the bedside, doesn't mean that there aren't answers in the lab. "That's why I do research."

Dr. Thébaud's current research focuses on bronchopulmonary dysplasia (BPD). This lung disease is most commonly diagnosed in premature infants who require a ventilator to breathe, because their lungs are not sufficiently developed to take in all the air they need. They must have supplemental oxygen to prevent brain damage and save their lives.

Although it seems contradictory, the oxygen and ventilation these babies so desperately need actually damage their lungs. The reason is that the lungs of premature infants should still be developing in the womb—which is, of course, a low-oxygen environment. The fetal lungs are filled with amniotic fluid and do not play a role in gas exchange. "Oxygen damages their lungs and interrupts normal lung development," says Dr. Thébaud. "The abnormal changes in the lungs of BPD infants mean they have

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difficulty getting the oxygen they need. BPD is very serious and can lead to respiratory failure."

Although there is currently no treatment for BPD, most babies do slowly improve, remaining prone to respiratory infections until they are about two years old. There is speculation that adults who had BPD at birth may have some lung function problems—another aspect that Dr. Thébaud will be exploring.

> "We need to know exactly how these drugs affect infant physiology"

"The fact that we have no treatment, combined with the increasing incidence of BPD (because of the increased survival rate of very-low-birthweight infants), means we must learn more about this disease," says Dr. Thébaud. His quest for knowledge has led him to fundamental research on two key aspects of lung growth: the development of the alveoli, the tiny air sacs in the lung where carbon dioxide and oxygen are exchanged; and the development of the network of tiny blood vessels that carries oxygen from the lungs into the bloodstream.

It was once thought that the process of blood vessel formation (called angiogenesis) simply followed the development of the alveoli. However, Dr. Thébaud's team and others have found evidence to suggest that angiogenesis drives the development of alveoli. This is an important finding because it opens up the possibility of a treatment for BPD. Although the high levels of oxygen given to premature babies arrest the development of alveoli, it may be possible to kick-start that development, even in an oxygenated environment, by promoting angiogenesis—perhaps with gene therapy.

"This idea is still far from clinical use," emphasizes Dr. Thébaud. "It's a proof of concept. But it does open some therapeutic options that might one day be a breakthrough to treat infants with BPD, as well as adult lung diseases in which alveolar damage occurs."

Like Dr. Thébaud, Heritage Clinical Investigator Dr. Po-Yin Cheung is a neonatologist and interested in the resuscitation of infants. Based at the University of Alberta, he does clinical and basic science research on the resuscitation of babies who have been deprived of oxygen at birth or as newborns. "I look at the recovery of organ function after resuscitation to see which interventions work best," explains Dr. Cheung.

For example, current guidelines advise giving pure oxygen to babies who need to be resuscitated. Dr. Cheung's findings challenge this directive. His work shows that a concentration of 21% oxygen—the concentration in normal room air—is just as effective as 100% oxygen in the short term. And in some circumstances, 100% oxygen can even be harmful.

Dr. Cheung is now extending this work to look at certain medications that support heart function in babies who are oxygen-deprived. "Currently, we go by results from adults and extrapolate them to children," he explains. "While this may work for older

children, organ function in babies is very different. In the NICU, we see complications after the initial sickness and we don't know if they were caused by the disease or the medicine. We need to know exactly how these drugs affect infant physiology."

Dr. Cheung is studying the function of two drugs that are commonly used to increase the strength of contractions in the hearts of very sick babies. "To raise blood pressure, we have to improve the heart function or constrict blood vessels. But the latter may restrict blood flow to organs, which is not what we want to do. In the NICU we measure blood pressure and heart rate, but we know virtually nothing about how much blood is going to the brain, the heart, the kidneys, or the gut. My experiments are aimed at understanding what really goes on in the organs of the body."

Dr. Cheung is also interested in following up on the long-term outcomes for these sick babies. "We need to look at how well our NICU graduates are doing years down the road. This is difficult to assess in the lab. At the end of this, I hope to be able to say which medications are better and how they should be used to give the best care to the babies we see in the NICU."

Of course, neonatologists like Drs. Cheung and Thébaud can't possibly sort out all the problems faced by infants in the NICU. Many other researchers, who are not physicians but scientists in related fields, are also searching for solutions. One of these is neurophysiologist and Heritage Scientist Dr. Klaus Ballanyi.

Arriving at the University of Alberta in 2002 from the University of Göttingen in Germany, Dr. Ballanyi was part of the international team that discovered the breathing centre in the brain stem. This group of cells generates a signal to the diaphragm, which makes it possible for us to breathe "automatically", without thinking about it. In Edmonton, Dr. Ballanyi studies the mechanisms of the central nervous system that underlie disturbances of respiratory rhythm just before and after birth.

"Babies who are facing life-threatening illnesses are often on opiates for pain or prostaglandins for heart problems," explains Dr. Ballanyi. "The problem with these drugs is that they depress breathing. So babies are often given another drug, such as caffeine, to stabilize breathing rhythms. The problem with these drugs is that they act throughout the body and can affect more than just breathing. The

ideal situation would be to find selective agents that act only to stabilize respiratory rhythms or reverse the respiration-depressing actions of drugs. That's where my work is focused."

Dr. Ballanyi's work is also applicable to sudden infant death syndrome (SIDS), the leading cause of death for babies between the ages of 28 days and one year. Its cause is unknown.

While the prospect of reducing the incidence of SIDS is exciting, Dr. Ballanyi emphasizes that his work is basic science, and quite far removed from application to patients. However, as a member of the University of Alberta's Perinatal Research Centre, he has the opportunity to work with physicians who do clinical research. "There's real support for collaboration between basic scientists and clinicians here in Alberta," he says. "It's a new environment for me and a very exciting one. Perhaps in a few years, I'll be able to work with others to apply what we have learned in the lab to developing a substance that can help babies with breathing problems."

Another basic scientist who is working on problems that face newborn babies is Heritage Senior Scholar Dr. Francine Smith at the University of Calgary. She focuses on the kidneys of the newborn.

Very little is known about the physiology of the newborn kidney, which is very different from that of the adult kidney. Dr. Smith's research aims to

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understand the normal processes that underlie kidney function during development. "The general view is that the newborn kidney is simply a little adult kidney," she says. "This is simply not the case at all."

By way of illustration, she explains that the kidneys of babies have very high vascular resistance, a measure of how the blood vessels resist the flow of blood. Vascular resistance is important because the blood supply to the kidneys controls how they function. High resistance at the outset means that there is very little in the way of a safety factor if resistance goes even higher, as can occur with hemorrhage or dehydration. This situation can be quite dangerous for the newborn baby, since the kidney can stop functioning completely. Premature infants are even more at risk because their kidney function is not as mature as that of babies born at full term.

Dr. Smith's approach is to try to figure out why the resistance is so high. "If we knew that, then perhaps we could lower it by using certain drugs," she says. "However, we must have the basic understanding first.

Dr. Francine Smith focuses on the kidneys of the newborn.

"Treatment of babies in the NICU inevitably involves controlling their fluid and electrolyte balance, regardless of whether their kidney function is normal or compromised. An understanding of the normal physiology of the developing kidney is vital to the advancement of new therapies."

For the past 10 years, one major focus in science has been at the cellular and molecular level, but Dr. Smith notes that the tide is turning. There is now a trend toward returning to integrative physiology—the study of the combined responses of tissues and organs as they affect the function of the major systems in the body—the kind of research carried out in her laboratory. "The human genome project is complete and now we need to increase our understanding of what these different genes actually do in a physiological sense," she says. "I think the next ten years will be a very interesting time for science and an exciting time for physiologists."

An ounce of prevention

We've all heard the warnings about smoking and drinking while pregnant, but many of us may not know that Alberta researchers are contributing important experimental data to these research areas. In particular, studies done by Dr. Robert Sutherland at the University of Lethbridge and Dr. Shabih Hasan at the University of Calgary are demonstrating serious short-term and long-term effects of prenatal drinking and smoking.

Dr. Sutherland, a Heritage Scientist and the director of the University of Lethbridge's Canadian Centre for Behavioural Neuroscience, is looking at prenatal alcohol exposure in rats and humans. His work on rats has already shown how the parts of the fetal brain involving memory and learning are permanently blunted by relatively low daily doses of alcohol. His team has measured neurochemical changes in the brain, as well as behavioural changes.

Now Dr. Sutherland is investigating whether the same brain changes and behavioural effects can be seen in humans. Preliminary data from a variety of non-invasive brain-imaging techniques show that there are indeed differences in the brains of people who were exposed to alcohol prenatally. It appears that the number of neurons is changed by prenatal exposure. "Extra neurons are associated with defects in the electrophysiology of the brain and memory," explains Dr. Sutherland. "At this point we don't know whether the changes in neurons are a direct effect of alcohol exposure or an indirect effect caused by the body trying to compensate for some other damage.

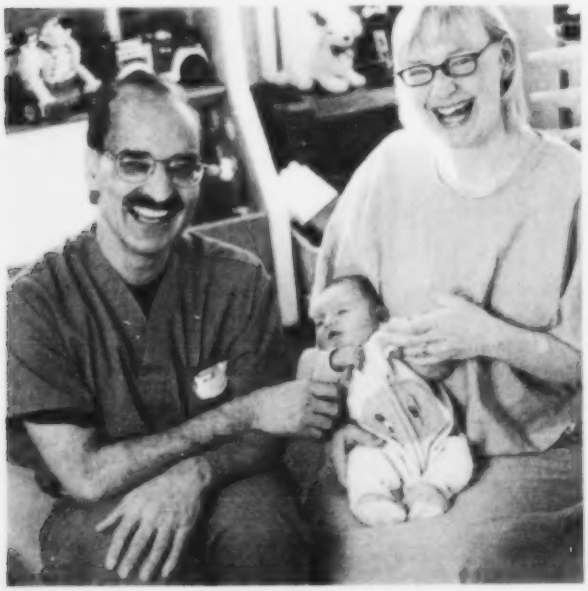
"Prenatal alcohol exposure has lifelong effects. It doesn't go away with time."

"What is clear from our research is that prenatal alcohol exposure has lifelong effects. It doesn't go away with time. It's not a developmental delay. Prenatal alcohol exposure is an injury, a pathology."

Could there be a cure? Perhaps, says Dr. Sutherland. "Any rational understanding of a pathological process gives us an idea of where to intervene to help. But at the moment, there's nothing. We can't correct the underlying neural defect because we don't yet know what it is.

"Education and prevention are key right now. If we look at the total cost to raise a child to age 21, it's estimated that in Canada we spend $1 million extra for every child who has been exposed to alcohol prenatally. Do the math and it very quickly makes sense to have prevention programs."

Another proponent of prevention programs is Heritage Scholar Dr. Shabih Hasan, a neonatologist at the University of Calgary. His research interest is breathing control in the fetus and the newborn. The findings from his research have convinced him of the need to educate women about the risks of smoking while pregnant.



Dr. Hasan's research team exposed rats to cigarette smoke prenatally and found that, once born, they had trouble with breathing regulation. In addition, when they were exposed to an environment with decreased oxygen, they experienced periods where they stopped breathing (apnea). The experiments included an exposure to heat stress, a risk factor implicated in sudden infant death syndrome (SIDS); when heat-stressed, the newborn rat pups developed prolonged periods of apnea and gasping breaths.

While this is a short-term effect that appears to resolve with age, the team's latest discovery highlights a disturbing long-term effect: The adult rats who were exposed to cigarette smoke prenatally have high blood pressure (hypertension). "It may be that the seeds of hypertension can develop in the womb," says Dr. Hasan. "This is a very significant finding." Even more intriguing is his observation that the coronary arteries do not relax well, which suggests that cigarette smoking during pregnancy "programs" the fetus for future ischemic (relating to reduced blood supply) heart disease. Dr. Hasan's team is now starting to look at the mechanisms behind these changes, and also whether the effects can be found in human infants whose mothers smoked while pregnant.

"My work on cigarette smoking shows serious short-term and long-term effects for babies," says Dr. Hasan. "As a doctor, I know that all the technology and the new drugs I have at my disposal cannot correct these problems. So the emphasis must be on prevention. The health of our children can be very much affected by what individuals do. Or don't do."

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AHFMR Clinical Investigator Dr. Bernard Thébaud is an assistant professor in the Department of Pediatrics and Child Health, Faculty of Medicine and Dentistry, University of Alberta. His research is also supported by the Canadian Institutes of Health Research (CIHR) and the Stollery Children's Hospital Foundation.

AHFMR Clinical Investigator Dr. Po-Yin Cheung is an assistant professor in the Department of Pediatrics and Child Health, University of Alberta. His research is also supported by CIHR, the Stollery Children's Hospital Foundation, the University Hospital Foundation, and the Royal Alexandra Hospital Foundation.

AHFMR Scientist Dr. Klaus Ballanyi is a full professor in the Department of Physiology and the Department of Pediatrics and Child Health at the University of Alberta. He is a member of the Perinatal Research Centre and the Centre for Neuroscience. His research is also supported by CIHR, the Canada Foundation for Innovation (CFI), and the Alberta Innovation and Science Research Investment Program (ISRIP).

AHFMR Senior Scholar Dr. Francine Smith is a full professor in the Department of Physiology and Biophysics and the Department of Medicine, University of Calgary. Her research is also supported by CIHR and the Heart and Stroke Foundation of Canada.

AHFMR Scientist Dr. Robert Sutherland is a full professor in the Department of Psychology and Neuroscience, Faculty of Arts and Sciences and Director, Canadian Centre for Behavioral Neuroscience, University of Lethbridge. His research is also funded by the U.S. National Institutes of Health (NIH), NSERC (Natural Sciences and Engineering Research Council of Canada), and the Canadian Stroke Network.

AHFMR Scholar Dr. Shabih Hasan is an associate professor in the Department of Paediatrics, Faculty of Medicine, University of Calgary. His research is supported by AHFMR, CIHR, the Alberta Lung Association, the Alberta Children's Hospital, Canadian Foundation for the Study of Infant Deaths, and SIDS Calgary Society.

Selected publications

Thébaud B, Barlier-Mur A-M, Chailley-Heu B, Henrion-Caude A, Tibboel D, Dinh-Xuan A-T, Bourbon JR. Restoring effects of vitamin A on surfactant synthesis in nitrofen-induced congenital diaphragmatic hernia in rats. *American Journal of Respiratory and Critical Care Medicine* 2001 Sep;164(6):1083-1089.

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Hasan SU, Simakajornboon N, MacKinnon Y, Gozal D. Prenatal cigarette smoke exposure selectively alters protein kinase C and nitric oxide synthase expression within the neonatal rat brainstem. *Neuroscience Letters* 2001 Mar 30;301(2):135-138.

AHFMR Clinical Investigator Dr. Bernard Thébaud is an assistant professor in the Department of Pediatrics and Child Health, Faculty of Medicine and Dentistry, University of Alberta. His research is also supported by the Canadian Institutes of Health Research (CIHR) and the Stollery Children's Hospital Foundation.

AHFMR Clinical Investigator Dr. Po-Yin Cheung is an assistant professor in the Department of Pediatrics and Child Health, University of Alberta. His research is also supported by CIHR, the Stollery Children's Hospital Foundation, the University Hospital Foundation, and the Royal Alexandra Hospital Foundation.

AHFMR Scientist Dr. Klaus Ballanyi is a full professor in the Department of Physiology and the Department of Pediatrics and Child Health at the University of Alberta. He is a member of the Perinatal Research Centre and the Centre for Neuroscience. His research is also supported by CIHR, the Canada Foundation for Innovation (CFI), and the Alberta Innovation and Science Research Investment Program (ISRIP).

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A quick search for parenting web sites or a trip down the Child Development aisle in a bookstore, and it's plain to see who most parenting information is aimed at—mothers. And that can leave fathers out in the cold, say Drs. Joyce Magill-Evans and Margaret Harrison, two University of Alberta professors who have collaborated for years on studies of children and families.

Wanted: dads

"Mothers tend to get all the attention," says Dr. Magill-Evans, an occupational therapist in the Faculty of Rehabilitation Medicine and a member of the Perinatal Research Centre. "We wanted to find out whether something can be done to make dads feel more comfortable and confident with their babies.

"From previous research, we know that dads interact differently with their babies. They engage in more physical play, and are less likely to use toy- or language-mediated play. There's nothing wrong with this; each type of interaction plays an important role in a child's development. But because the way dads play with babies is not usually discussed, men can feel less confident."

Supported by a grant from the Health Research Fund, the researchers have designed and tested an intervention to help first-time dads. (They don't want to reveal the nature of the intervention for fear of biasing the results.) A full-scale study is underway, and volunteers—first-time dads whose babies are less than five months old—are being recruited now. Every father in the study will receive a series of home visits; some will receive the intervention, and some will not.

Dr. Harrison, who is a professor in the Faculty of Nursing, notes that the study is timely because there is growing demand from fathers for this type of information. "Dads are taking a more active role in bringing up their babies; some are the primary caregivers," she says. "But dads don't tend to go to parenting groups, and they have limited opportunities for feedback on how they're doing. We hope we're laying the groundwork to keep fathers involved with their children."

First-time fathers of babies under 5 months old are being recruited for this study in Calgary and Edmonton. If you would like to know more, call 403-220-8058 or 780-492-0402.

Dr. Joyce Magill-Evans is a full professor in the Department of Occupational Therapy, Faculty of Rehabilitation Medicine, University of Alberta. Her research is supported by the Health Research Fund, which is administered by AHFMR on behalf of Alberta Health and Wellness. She also receives funding from CIHR.

Dr. Margaret Harrison is a full professor in the Faculty of Nursing, University of Alberta. Her research is also supported by the Health Research Fund and CIHR.

Selected publication

Boechler V, Harrison MJ, Magill-Evans J. Father-child teaching interactions: the relationship to father involvement in caregiving. *Journal of Pediatric Nursing* 2003 Feb;18(1):46-51.

ABOVE: DR. JOYCE MAGILL-EVANS AND DR. MARGARET HARRISON

Transport

Talk to University of Alberta physiology professor and Heritage Scientist Dr. James Young for a while, and you'll learn that collaboration with colleagues near and far is very important to him. He came to Edmonton 13 years ago from the Chinese University of Hong Kong largely because he was already working closely with researchers at the U of A.

In his work on cell membrane proteins, he continues to collaborate with colleagues within his own department and in other departments. In fact, the CIHR Membrane Protein Research Group, which he helped create and co-directs, brings together researchers from all around the Faculty of Medicine and Dentistry to pursue research on membrane proteins. Dr. Young considers it to be one of the foremost centres of membrane research in the world; and in 2001, the University of Alberta recognized the group as one of its areas of international scientific excellence.

"What we've achieved is an extensive network of collaborative interactions," says Dr. Young, "and that really is one of the main attractions of working here at the U of A—the ability to interact with different people and extend research beyond your own borders."

Dr. Young studies proteins in cell membranes that transport nucleosides and nucleobases (the forerunners of nucleotides, which in turn are the building blocks of DNA and RNA) into and out of cells. His laboratory in the physiology department uses molecular biology techniques to identify and isolate these proteins. Most of the work is done by injecting genetic messages for the membrane proteins from humans, other animals, and even bacteria such as *E. coli*, into unfertilized eggs of *Xenopus Laevis*, the South African clawed frog. This allows the biological machinery of the egg cells to be used to produce membrane proteins for further study. In addition, the lab team just started "knockout" studies on mice and worms, where the genes for specific membrane proteins are deleted from the genetic makeup of the organism to see what happens to the organism when they aren't present.

proteins

"Ultimately those kinds of experiments are critical to the long-term goal of really understanding what these proteins and protein families do," Dr. Young says.

In his lab a team of skilled and dedicated investigators and research trainees have discovered two new families of membrane transport proteins: equilibrative and concentrative nucleoside transporters (ENTs and CNTs). ENTs shepherd the movement of nucleosides and nucleobases across the cell membrane; some ENTs may act inside the cell, as well. CNTs are different from ENTs in that they have the ability to actively pump nucleosides across the cell membrane into the cell.

In humans, some cells can make nucleobases and nucleosides, but many can't (for example, red and white blood cells, bone-marrow cells, and some brain cells). Those that can't have to scavenge precursors already present in the body—derived from the diet or produced by organs such as the liver—and bring them into the cell via the membrane transport proteins.

"What we've achieved is an extensive network of collaborative interactions"

Dr. Young believes that basic research on transport proteins will bring about a better understanding of their individual roles in the whole organism. On a practical level, he expects it will lead to improvements in chemotherapy for cancer patients and for those with such life-threatening viral infections as AIDS and hepatitis. Many synthetic nucleoside drugs currently in use for chemotherapy work by entering cells via nucleoside transport proteins. They are then incorporated into the DNA and RNA, where they eventually block DNA and RNA synthesis and kill the cancer or virally infected cell. The research also has implications for pain control, inherited neurodegenerative disease, and parasite chemotherapy for diseases such as malaria.

A native of Scotland, Dr. Young spent almost a decade in Hong Kong before making the move to the University of Alberta in 1990. Between the summer of 1982 and the spring of 1986, Dr. Young had come to the U of A five times as a visiting professor or speaker sponsored by AHFMR. During that time he established collaborations with professors Dr. Alan Paterson (now a professor emeritus of pharmacology) and Dr. Carol Cass (now director of the Cross Cancer Institute in Edmonton). "These interactions became stronger over the years and of course when I came to visit, I also established interactions with other people," says Dr. Young. "It reached a stage where it made logical sense to make a move to the U of A." When the university invited him to relocate permanently to Edmonton, AHFMR provided funds to help bring him from Hong Kong and start up his lab and has funded him ever since.

"I think it was a great move," says Dr. Young. "Looking back, our original optimism has been fully borne out by what we've been able to accomplish."

Dr. James D. Young, a professor in the Department of Physiology at the University of Alberta, is a Heritage Scientist and also receives funding from the National Cancer Institute of Canada, the Alberta Cancer Board, and the Canadian Institutes of Health Research.

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Yao SYM, Ng AML, Vickers MF, Sundaram M, Cass CE, Baldwin SA, Young JD. Functional and molecular characterization of nucleobase transport by recombinant human and rat equilibrative nucleoside transporters 1 and 2: chimeric constructs reveal a role for the ENT2 helix 5–6 region in nucleobase translocation. *Journal of Biological Chemistry* 2002 Jul 12;277(28):24938-24948.

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Social support and health

When Marlene Bidgood's husband was discharged from hospital four months after suffering a stroke, the reality of her new life as a caregiver hit hard. "Over the next five years I became totally burned out, lost my job, and my life became a mess. I had very little social support."

Social support is absolutely vital, not only to feeling loved, valued, and secure, but also to our health and well-being, says Heritage Senior Health Scholar Dr. Miriam Stewart. Scientific director of the Institute of Gender and Health (one of the Canadian Institutes of Health Research) and former director of the University of Alberta's Centre for Health Promotion Studies, Dr. Stewart launched the Social Support Research Program at the University of Alberta. This $2.6-million multidisciplinary research effort has projects throughout Alberta and across Canada.

Social support refers to the various types of support that people receive from others. It can come from family, friends, co-workers, neighbours, health professionals, and others. "It can also come from people who have been in the same situation–we call them peers. Much of our work focuses on support interventions given by peers and professionals," says Dr. Stewart.

For example, one study assessed telephone support for new family caregivers of seniors with chronic health conditions; specifically, stroke survivors and those afflicted with Alzheimer's disease. Weekly telephone support calls were made by trained peer helpers–experienced family caregivers–who offered information, affirmation, and emotional support in Edmonton, Calgary, and central Alberta.

"Based on our previous research, we know that people in stressful situations benefit from the experience and knowledge of peers as well as professionals," says Dr. Stewart. "Often the support from family and friends is insufficient during stressful times and/or it diminishes over time. Peer support can make a big difference."

Marlene Bidgood was one of the peer-support providers. She mentored six caregivers during the course of this project. "I joined the peer support team eight years after my husband had his stroke," she says. "I was disappointed to find that so very little had changed for caregivers. The people I mentored were all trying to cope with a role they were not at all prepared for. It made me realize that caregivers need a safe place to talk. What place is safer than with a person who truly knows what you are going through? This project was an incredible idea."

Although the caregiver support project was completed in 2002, its success inspired Marlene to start the Alberta Caregivers Association. This non-profit organization educates, advocates, and networks on behalf of people caring for an adult with a chronic illness. Its mission is to help primary caregivers maintain as much of their normal lives as possible.

The Heritage Foundation was the key funder of the caregiver peer-support study. "AHFMR has been a major funder of many of our projects, as well as providing support for me as a Senior Health Scholar," notes Dr. Stewart. "This support has been critical to the success of the research program because it allowed

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time to develop proposals and work on assembling multidisciplinary research teams and staff. Consequently, we've been very successful in attracting funding from 10 other national and provincial agencies for 10 projects. AHFMR deserves a lot of credit."

Another study (co-funded by AHFMR and the Canadian Institutes of Health Research) assesses on-line computer support for adolescents with cerebral palsy and spina bifida. Like the caregiver support study, it builds on earlier work done by Dr. Stewart and colleagues in a research program emphasizing social support for caregivers in Nova Scotia.

"Our previous work revealed that adolescents with spina bifida had much greater support needs and isolation from peers than children and adolescents with some other chronic health conditions," she explains. "So we were eager to work with this group again."

The first phase of the project was a telephone survey to determine support needs and patterns of computer use among adolescents with spina bifida and cerebral palsy. The adolescents reported a high level of computer use and a desire to communicate with other teens with the same disabilities. A six-month on-line support intervention, including e-mail, message boards, and chat rooms, was planned for the second phase. Peer mentors (young adults with the same condition) and health professionals offered support on-line. The project, conducted in both Calgary and Edmonton, is nearing completion.

"This kind of support is desperately needed. There are many groups who are vulnerable for health risks and support deficits–such as people with chronic health conditions, family caregivers, people living on low incomes, homeless people, immigrants, and refugees."

The Social Support Research Program has fostered enormous research capacity. Dr. Stewart has assembled a superb program team of 47 investigators from a wide range of disciplines. The projects are all based in Alberta, but many also engage researchers from other provinces. As well, nearly 50 Alberta-based graduate students (master's and Ph.D.) and recent graduates have been involved in the program over the past four years.

"In addition to training researchers, our work builds capacity in the communities," says Dr. Stewart. "For example, low-income people were trained to conduct interviews of other low-income people; former homeless youth to work with homeless youth; young adults with disabilities to offer support to adolescents; and experienced family caregivers to provide support to new family caregivers of seniors with chronic health conditions."

Most of the recent work of the Social Support Research Program has focused on the links between social support and other factors that influence health (health determinants); in particular, ethnicity, socio-economic status, and gender. This focus dovetails with Dr. Stewart's appointment as scientific director of the Canadian Institutes for Health Research (CIHR) Institute of Gender and Health.

"What excites me is moving beyond assessment: using the assessments to guide the design of interventions, testing interventions, and ultimately attracting the interest of people who develop services, programs, and policies."

Dr. Stewart is an AHFMR Senior Health Scholar and a professor in the Faculties of Nursing and Medicine at the University of Alberta. Funding for projects in the Social Support Research Program comes from many sources, including AHFMR; Canadian Health Services Research Foundation; Canadian Institutes of Health Research; Health Canada; the Social Sciences and Humanities Research Council of Canada; United Way of Alberta; Boyle McCauley Health Centre; Capital Care; and the Edmonton Community Lottery Board. Dr. Stewart also receives funding from the Health Research Fund, which is administered by AHFMR on behalf of Alberta Health and Wellness.

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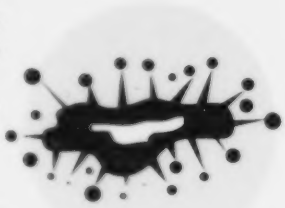
AHFMR Scholar Dr. Steven Mosimann is not trying to solve one specific health problem or disease with his research, which focuses on controlling the amount of protein that's present in a cell. Instead, the University of Lethbridge scientist is looking for ways to improve the treatment for many problems.

Learning not to shoot the **messenger**

Dr. Mosimann explains that a cell is like a factory that has to be able to produce many different things at different times. In order to do this, cells produce their own specialized workers—proteins—each of which does its own specific job or limited range of jobs. The DNA acts as head office and is a list of all the available workers and their jobs. When the factory needs to produce something new, it first makes a set of messenger RNAs (mRNAs). These are the messages from head office requesting production of the set of specific proteins (workers) needed to do the job. The mRNAs have an important property that makes them different from the genes and proteins: they have a very short lifetime. "Think of it as the foreman crumpling up the message from head office as soon as he reads it," says Dr. Mosimann. "The cell uses and rapidly degrades mRNA because it must be able to respond really rapidly to changes."

For years people have studied gene regulation—controlling whether the message is sent, in order to control the amount of that protein and what the cell produces. "While this has worked very well, we've never achieved the level of control that we want," says Dr. Mosimann. "The cell has regulatory mechanisms (sensors) which tell it when it has enough of a particular protein and it stops sending the message." He explains that one way to achieve higher protein levels without affecting the expression of the gene is to look at the lifetime of the message. "We want to stop the foreman from crumpling up the message and throwing it in the garbage, so that he will continue following its instructions. In order to do this, we want to understand why the message gets thrown out."



Dr. Mosimann explains that everything in biology, chemistry, and physics tells us that the three-dimensional shape of something is intimately related to its physical properties and its biological function. "If we can understand the shape of the molecules whose job it is to destroy these messages, then we can begin to understand and control how they are broken down," he says. "We're trying to determine, at atomic-level resolution, the shape of several of the proteins that are known to degrade mRNA. Once we know that, we should be able to understand how these proteins and messenger RNAs interact, and we can begin unlocking the secrets of what controls the message's lifespan."

Learning to control protein expression can make all of today's current biotechnology and genetic therapy approaches more powerful, Dr. Mosimann says.

Messenger RNAs (mRNAs) are the messengers from head office.

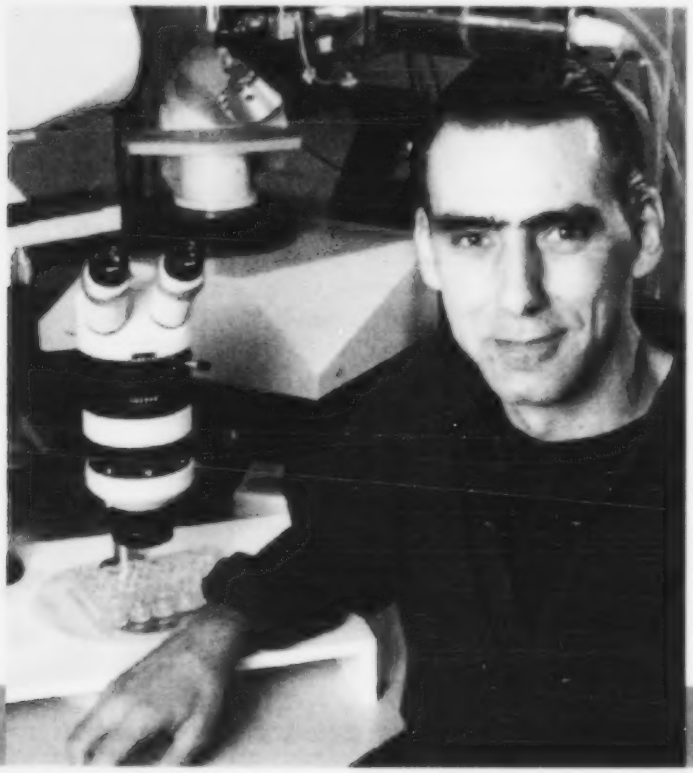
He explains that genetic mutations leading to disease or sickness are often the result of a protein that isn't shaped properly, and thus can't do its job correctly. Gene therapy aims to fix the problem by introducing a healthy copy of the gene obtained from somebody else. But because the patient then has two copies of the gene present, only 50% of the protein will be produced by the healthy gene. "A cell is exquisitely balanced and it doesn't want any additional protein," says Dr. Mosimann. "Our technology would allow us to produce more protein than the regulatory mechanism would normally allow, sidestepping the head-office order to shut down the assembly line."

Genetic mutations are often the result of a protein that isn't shaped properly.

Dr. Mosimann collaborates with another research group that is trying to change the amount of fat present in canola oil. They have introduced an extra gene into canola cells to produce more of the healthy type of fat (polyunsaturated). At present, regulatory mechanisms in the cell limit the amount of healthy fat present in the oil. With the technology Dr. Mosimann is working on, this research group could override those mechanisms and allow production of the healthy fat to continue. "Biotechnology and genetic therapy are about controlling the amount of a given protein that is in a cell at a time. We want to provide a finer level of control."

Dr. Mosimann uses protein crystallography for his studies; in other words, he takes pictures of proteins. Using what is essentially an x-ray light bulb (obtained with Heritage funding), he shoots x-rays at crystals. The interaction between the x-rays and the molecules that make up the crystals changes the paths of the x-rays. This information is then captured and computers are used to calculate and create the image. "We have to use a crystal to determine a three-dimensional picture for two reasons. First, you can't hold a single molecule steady and take a picture from all angles; and second, a single molecule doesn't scatter enough x-rays for us to detect. So we grow a crystal that is made up of an enormous number of molecules." Synchrotrons reduce the mathematical calculation needed in crystallography and allow researchers to use smaller crystals. Once Canada's first synchrotron, the Canadian Light Source (CLS), opens in Saskatoon in 2004, Dr. Mosimann will be able to send his crystals there.

The University of Lethbridge had no crystallography facilities when Dr. Mosimann arrived at the end of 2000, and he faced the long process of setting up his lab from scratch. But Lethbridge also offered the quality of life of a smaller centre, a chance to remain on the Prairies—and future access to the CLS. "For me, it was the best opportunity," he says.



AHFMR Scholar Dr. Steven Mosimann is an assistant professor in the Department of Chemistry and Biochemistry at the University of Lethbridge. He also receives funding from NSERC (Natural Sciences and Engineering Research Council of Canada) and the Canada Foundation for Innovation.

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Luo Y, Pfuetzner RA, Mosimann S, Paetzel M, Frey EA, Cherney M, Kim B, Little JW, Strynadka NCJ. Crystal structure of LexA: a conformational switch for regulation of self-cleavage. *Cell* 2001 Sep 7;106(5):585-594.

Mosimann SC, Gilbert M, Dombrowski D, To R, Wakarchuk W, Strynadka NCJ. Structure of a sialic acid-activating synthetase: CMP-acylneuraminate synthetase in the presence and absence of CDP. *Journal of Biological Chemistry* 2001 Mar 16;276(11):8190-8196.

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Fish oils and the fight against breast cancer

PATRICIA SCHLEY

High in protein, low in saturated fat, and valuable in protecting against heart disease, fatty fish such as salmon, tuna, and herring get top marks in the world of nutrition. Now research at the University of Alberta is exploring yet another health advantage associated with the omega-3 fatty acids found in these fish: the role they play in the battle against breast cancer.

Patricia Schley, an AHFMR Student and Ph.D. candidate in the Department of Agricultural, Food and Nutritional Science, is trying to find the link between fish oils and breast-cancer cell growth. "We know that exposing breast-cancer cells to the omega-3 fatty acids found in fish can inhibit the cells' growth," she says. "We also know that dietary omega-3 fatty acids decrease tumour growth in animal models of breast cancer. The important question is: how do these fish oils do it?"

Using two different breast-cancer cell lines—one representing a slow-growing, earlier stage of cancer and the other a more aggressive later stage—Patricia is close to finding the answer. By incorporating eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) into the substance that bathes and feeds the breast-cancer cells, she can measure the effects of these omega-3 fatty acids.

"At first we thought that perhaps EPA and DHA were slowing down or stopping breast-cancer cell division, but looking at all the different stages of cell growth, this doesn't appear to be the case." Instead of stopping cell development, the omega-3 fatty acids actually kill the cancer cells. Patricia has discovered that EPA and DHA become incorporated into the membranes of the breast-cancer cells and may be pre-

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venting the cells from sending signals that promote their survival. "Down the road, we will use animal models to see if fish oils inhibit mammary-tumour growth by the same mechanisms as in the cell lines. And ultimately, human studies will be necessary to determine whether fish oils can be of benefit in controlling the growth of breast cancers."

Originally from British Columbia, Patricia had her first experience with cancer research in 1998 when she did a co-op term at the BC Cancer Research Centre. Her interest in working with supervisor Dr. Catherine Field brought her to the University of Alberta. "I love working in Dr. Field's lab. It's very easy to make the link from the research that I do to the benefits it may have on individuals suffering with breast cancer. This research lends credibility to the use of fish oils as anti-cancer agents. Our goal is to figure out how these fatty acids work, which may help us understand if and how they'll interact with other breast-cancer drugs. Ideally, one day omega-3 fatty acids could be used in conjunction with other drugs to fight breast cancer."

AHFMR Student Patricia Schley is a Ph.D. candidate in the Department of Agricultural, Food and Nutritional Science at the University of Alberta. She has also been awarded the Andrew Stewart Memorial Graduate Prize and is an honorary recipient of the University of Alberta Dissertation Fellowship.

Selected publications

Schley PD, Field CJ. The immune-enhancing effects of dietary fibres and prebiotics. *British Journal of Nutrition* 2002;87 Suppl 2:S221-S230.

Field CJ, Schley PD. Evidence for potential mechanisms for the effect of conjugated linoleic acid on tumor metabolism and immune function: lessons from omega-3 fatty acids. *American Journal of Clinical Nutrition.* In press 2003.

Correction

The fall 2003 story "The healthy community" incorrectly identified Dr. Penelope Hawe as the Markin Chair in Health Promotion. The correct title is the Markin Chair in Health and Society.

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Research views

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University of Alberta Perinatal Research Centre
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Dr. Francine Smith's web site
http://www.ucalgary.ca/~fsmith/francine_s.html

University of Calgary Respiratory Research Group
http://www.ucalgary.ca/~resprg/

Transport proteins

Dr. James Young's web site
http://www.physiology.ualberta.ca/Young.htm

Social support and health

The Social Support Research Program
http://www.ssrp.ualberta.ca/

Alberta Caregivers Association
http://www.albertacaregiversassociation.org/

Learning not to shoot the messenger

Dr. Steven Mosimann's web site
http://people.uleth.ca/~steven.mosimann/

Canadian Light Source Inc.
http://www.cls.usask.ca/

Talib Rajwani

2003–2004 Lionel E. McLeod Scholarship winner

Talib Rajwani has spent several months in India educating high school kids about HIV. He's helped develop a program to teach elementary kids about the dangers of smoking. He's volunteered his time for such causes as cystic fibrosis research, diabetes awareness, sexual education, and women's shelters. He's won a world debate and public speaking championship, been named one of the 100 Canadians to watch for by Maclean's magazine, and somewhere along the way, has still found time to do some first rate health research. And how does the winner of the 2003-2004 Lionel E. McLeod Health Research Scholarship manage to fit in all of these things? "I am very passionate about the activities that I am involved in," he says, shrugging off the question. "Activities like these blur the line between work and my personal interests."

Talib is a medical student in the MD-PhD program at the University of Alberta, a program that allows students to do PhDs between their second and third years of medical school before finishing their medical degrees. In an interdisciplinary PhD project involving the Departments of Radiology and Surgery and the Faculty of Rehabilitation Medicine, Talib is examining the causes of adolescent idiopathic scoliosis—a curvature of the spine that affects about 3% of adolescents between 11 and 17. He explains that while the condition is fairly common, the causes of about 80% of the cases are unknown. A better understanding of the causes of scoliosis could lead to earlier and more preventative treatments.

Talib's research is concerned with the uneven development of two growth plates in the spine—the neurocentral junctions. Initially, it was thought that these growth plates closed too early in a child's life to be a factor in adolescent scoliosis, but MRI evidence shows that they remain open much later in life than previously believed. "We're using MRI and other tools to examine the neurocentral junctions, understand the role they play in vertebral growth, and determine if uneven growth at these sites leads to scoliosis," says Talib. "More importantly, we are developing a model for how scoliosis research should be conducted. After hundreds of years of research, almost everyone in this field would concede that we are far from developing a cure. One of the major problems is that because there appears to be many different causes for scoliosis, investigating one particular cause in a random sample of patients is difficult. At the same time, the determination of cause and effect relationships requires animal and computer based models in addition to human studies."

Talib plans to become a clinical investigator when finished his double degree, and hopefully practice in radiology. "I'm a naturally inquisitive person when it comes to the way the world works," he explains of his plans to continue in research. "I think that's a fundamental characteristic that all researchers share—an analytical mind and a question-based approach that focuses on why things work the way they do. In my opinion, the greatest asset that any researcher can have is an insatiable sense of curiosity."

Talib Rajwani is an MD-PhD student in the University of Alberta Medical Sciences program through the Department of Radiology and Diagnostic Imaging. He has won numerous awards and scholarships during his academic career, including an Alberta Science and Technology (ASTech) Leaders of Tomorrow award.

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